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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,425	01/26/2001	Xaveer Van Ostade	4644US	8053

7590 06/24/2004

Allen C. Turner
TRASK BRITT
P.O. BOX 2550
Salt Lake City, UT 84110

EXAMINER	
LI, RUIXIANG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/771,425	OSTADE ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,14-16,18 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-11, 14-16, 18, and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/29/2004 &12/04/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

The Request filed on March 29, 2004 for Continued Examination (RCE) under 37 CFR 1.114 of Application 09/771,425 is granted. An action on the RCE follows.

Applicants' Amendment and Claims

Applicants' amendment filed on March 29, 2004 has been entered in full. Claim 2 has been canceled. Claims 1, 3-11, 14-16, 18, and 21-25 are pending and under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Withdrawn Rejections

Applicants' cancellation of claim 2 has made the rejection of the claim under 35 U.S.C. 103(a) as being unpatentable over Pestka et al. (WO 98/02558) in view of Trueheart et al. (WO 98/13513) as set forth in Paper No. 20 moot.

The rejection of claims 15 and 18 under 35 U.S.C. 112, 2nd paragraph set forth in the record (Paper No. 20) has been withdrawn in view of Applicants amendment to the claim.

Information Disclosure Statement

The information disclosure statements filed on 12/04/2003 and 03/29/2004 have been considered by the Examiner and a signed copy of the form PTO-1449 is attached to the office action.

Objection to Abstract

The abstract of the disclosure is objected to because of the presence of typed materials, which are not related to the disclosure. Correction is required. See MPEP § 608.01(b).

Claim Rejections Under 35 U. S. C. § 112, 2nd paragraph

The rejection of claims 11, 16, 24, and 25 under 35 U.S.C. 112, 2nd paragraph set forth in the record (Paper No. 20) is maintained.

Amended claim 11 remains to be indefinite because the steps set forth in the method do not necessarily achieve the goal set forth in the claim preamble. Specifically, a step of determining or measuring binding is missing. In addition, it is unclear, as the claim is written, whether the test compound and/or ligand are encoded in the mammalian cell of claim 1. It is also suggested that "thus screening for" be amended as "thereby identifying".

The amended claim 24 remains to be indefinite because the steps set forth in the method cannot achieve the goal set forth in the claim preamble. It is unclear how an

antagonist could be identified by determining the ability of the compound to activate the reporter system. It appears that expression of an inhibitor would create an anti-autocrinic loop, instead of autocrinic loop (see, e.g., top of page 8 of the instant specification). In addition, claim 24 recites "a positive or a negative control". It is unclear what the metes and the bound of the term are. Neither the specification nor the claim defines the term unambiguously, rendering the claim indefinite. Furthermore, claim 16, which depends upon claim 24, recites "said ligand comprises a gene encoding said antagonists", which is confusing. It is unclear how a ligand can comprise a gene encoding an antagonist.

Amended claim 25 remains to be indefinite because it recites "a positive or a negative control". It is unclear what the metes and the bound of the term are. Neither the specification nor the claim defines the term unambiguously, rendering the claim indefinite. In addition, claim 25 recites the limitation "said series of compounds " in line 12 of the claim. There is insufficient antecedent basis for this limitation in the claim. Furthermore, while the activation of the reporter system may indicate whether a compound is an agonist or an antagonist, it does not indicate whether a compound binds to the receptor or inhibits the ligand-receptor binding.

Claim Rejections Under 35 U. S. C. § 103 (a)

(i) The rejection of claims 1, 3-6, 10, 11, 14-16, 18, and 21-25 under 35 U.S.C. 103(a) as being unpatentable over Pestka et al. (WO 98/02558, January 22, 1998) in view of

Trueheart et al. (*IDS*, WO 98/13513, April 2, 1998), set forth in Paper No. 20, is maintained.

Beginning at the bottom of page 8 of the Applicants' response, Applicants argue that a *prima facie* case of obviousness cannot be established with regard to any of independent claims 1, 15, 24, or 25 as amended, since the cited references do not, alone or in combination, teach or suggest each and every element of any of the independent claims or any of the claims depending therefrom. For instance, the asserted combination of the chimeric receptor of Pestka et al. with the yeast cells of Trueheart et al. does not result in the cells recited in any independent claims 1, 15, 24 or 25.

This has been fully considered but is not deemed to be persuasive because the previous Office action (Paper No. 20, June 11, 2003) clearly indicates how the cited references in combination teach or suggest the claimed invention. Pestka et al. teach expression of various chimeric receptors in COS-1 cells (Fig. 2); Hu-IL-10R/γR1 chimeric receptor in hamster cells; EpoR/γR1 and EpoR/γR2 (erythropoietin-interferon γ receptors) in CHO-16-9 cells (Fig. 15). In these examples, the cytoplasmic part of the chimeric receptor is a cytoplasmic part of interferon γ receptor. In response to IL-10, the Hu-IL-10R/γR1 chimeric receptor was activated and HLA-B7 surface antigen in hamster cells was induced (Example 2). Likewise, on activation by EPO which was exogenously added to cells, the chimeric receptor formed homodimers or heterodimers and the cells

expressing the chimeric receptor exhibited enahnced class I MHC antigen expression (Example 3). Trueheart et al. teach expression of a large number of polypeptides in a library in a cell to identify those polypeptides that agonize or antagonize receptor bioacitivity, creating an autocrine system (page 3, last paragraph; page 51). Trueheart et al. also teach expression systems (expression vectors, promoters, etc.) used for production of polypeptides in a cDNA library (See, page 22, expression systems). The specific examples refer to activation of the pherome pathway in yeast by heterologous receptors, however, Trueheart et al. also clearly teach that other cells, including mammalian cells, can be used as host cells (see page 2, last paragraph or page 20). Based upon these teachings, it would have been obvious to one having ordinary skill in the art at the time the invention was made, as a matter of choice, instead of exogenous addition of a test compound to cells, to use a second gene encoding a compound taught by Trueheart et al. so that a compound can be expressed, an autocrine or anti-autocrine loop can be created in cells taught by Pestka et al., and such cells can be used for the screening method taught by Pestka et al. with a reasonable expectation of success.

At the middle of page 9 of the Applicants' response, Applicants argue that since each of the working examples of Trueheart et al. is limited to the use of yeast cells, one skilled in the art would not reasonably expect the chimeric receptor of pestka et al. to function in the yeast cells of Trueheart et al. For instance, one skilled in the art would not expect the autocrinic loops including the G-protein coupled receptors of the yeast cells of Trueheart et al. to function in the cells of Pestka et al. in the same manner as a test

compound exogenously added to a cell since the cells of pestka et al. include several hundreds of GPCRs. At the beginning of the 2nd paragraph of page 10, Applicants argue that since the receptors of Trueheart et al. are functionally integrated in the signaling pathway, e.g., the endogenous signaling pathway, the chimeric receptor of pestka et al. would not be expected to work in the yeast cells of Trueheart without undue experimentation or testing.

This has been fully considered but is not deemed to be persuasive for the following reasons. Pestka et al. teach expression of various chimeric receptors in COS-1 cells (Fig. 2); Hu-IL-10R/γR1 chimeric receptor in hamster cells; EpoR/γR1 and EpoR/γR2 (erythropoietin-interferon γ receptors) in CHO-16-9 cells (Fig. 15) and methods for identifying a specific ligand, an agonist, or an antagonist using routine screening techniques and a highly sensitive assay cell line that express a chimeric receptor, whereas Trueheart et al. teach expression of a large number of polypeptides in a library in a cell to identify those polypeptides that agonize or antagonize receptor bioactivity, creating an autocrine system. Trueheart et al. not only teach activation of the pheromone pathway in yeast by heterologous receptors, but also teach the use of other types of cells, including mammalian cells, as host cells and the use of several target receptors such as cytokine receptors, receptor tyrosine kinases, and G-protein coupled receptors. With the extensive teachings in the art, including those of Pestka et al. with Trueheart et al., the claimed invention as a whole would have been obvious to an artisan. One skilled in the art would be able to combine the chimeric receptors taught by

Pestka et al. with the autocrinic loops taught by Trueheart et al. in different ways with a reasonable expectation of success. The Examiner notes that Applicants' argument is equivalent to argue that the instantly claimed invention is not enabled in its full scope because the instant claims are drawn to a mammalian cell comprising a chimeric receptor or a screening method of using the cell, whereas a chimeric receptor encompasses any chimeric receptors, e.g., GPCRs.

At the bottom of page 9, Applicants argue that Trueheart et al. recognize that wild-type gene would frustrate genetic selection because of the background produced by the wild-type gene, and thus teaches away from combining the teachings of Trueheart et al. with Pestka et al. Applicants further argue that the mammalian cells of Pestka et al. would be expected to produce a background that would frustrate selection.

This has been fully considered but is not deemed to be persuasive because an artisan would be able to evaluate the background to determine whether it is appropriate to use a specific phenotype or a mammalian cell for the screening method, with the extensive teachings of Pestka et al. and Trueheart et al. Thus, the recognition of potential background produced by a wild-type gene does not teach way from combining the teachings of Trueheart et al. with Pestka et al. Furthermore, neither the art nor the references cited by Applicants provide teachings that expression of a second gene encoding a test compound as taught by Trueheart et al. in the mammalian cells

expressing a chimeric cytokine receptor taught by by Pestka et al. to create an autocrine or anti-autocrine loop would produce a background and frustrate selection.

At the 2nd paragraph of page 10 of Applicants' response, Applicants argue that the article submitted herewith provides additional evidence that the autocrinic loop of Tureheart et al. would not be expected to work with the mammalian cells of Pestka et al.

This has been fully considered but is not deemed to be persuasive because Applicants' argument in incorrect. Browder et al. clearly teach endogenous expression of the IL-3 gene introduced with a retrovirus vector creates an autocrine stimulation in hematopoitic cells and that endogenously produced IL-3 interacts with its receptor (see, the title and abstract of the reference).

(ii) The rejection of claims 7 and 8 under 35 U.S.C. 103(a) as being unpatentable over Pestka et al. (WO 98/02558, January 22, 1998) in view of Trueheart et al. (WO 98/13513, April 2, 1998), and further in view of Pellegrini et al. (*Molecular and Cellular Biology* 9:4605-4612, 1989), as set forth in Paper No. 20, is maintained.

(iii) The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Pestka et al. (WO 98/02558, January 22, 1998) in view of Trueheart et al. (WO 98/13513, April 2, 1998), and further in view of Mizushima et al. (Nucleic Acids Research, 18:5322, 1990), as set forth in Paper No. 20, is maintained.

It is noted that Applicants did not argue about the rejections (i) and (iii).

Claim Objections

Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 18 recites the limitation that agonists are produced by the autocrinic loop. However, such a limitation is already present in the mammalian cell recited in claim 15.

It is suggested that "thus screening for" in claim 15 be amended as "thereby identifying" for clarity.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (571) 272-0887.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [Gary.Kunz@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Ruixiang Li

Ruixiang Li, Ph.D.
Examiner
June 21, 2004